

TOBACCO INDUSTRY RESEARCH COMMITTEE

350 Fifth Avenue, New York 1, N. Y.

Application for Research Grant

Date: April 27, 1956

1. Name of Investigator:

Richard L. Wechsler, M. D.

2. Title:

Clinical Physiologist

3. Institution & Address:

Montefiore Hospital Institute of Research
3459 Fifth Avenue, Pittsburgh 13, Pennsylvania

4. Project or Subject:

Effect of Cigarette Smoking and Intravenous Nicotine on Cerebral Blood Flow, Cerebral Metabolism, Blood Gases, Blood pH, Arterial Pulse Pressure Curves, Electrocardiograms, and Electroencephalograms in People of the Older Age Group with Arteriosclerosis. Studies during the past 9 months have failed to show any significant tobacco effects on cerebral blood flow or metabolism in young men. At the Tobacco Committee Conference in New York (March 16, 1956), the investigation of cigarette effects or intravenous nicotine effects on human brains of older people was discussed and suggested. In addition, the effects of denicotinized cigarettes will be studied.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

Patients or paid subjects over 60 years of age will be chosen at random from the hospital or general population. All will be people who smoke cigarettes, but a 12 hour period of abstinence from smoking will be observed. The studies will be accomplished in the morning with the subjects in a fasting state at bed rest in the supine position. A 30 minute rest period will precede the control or "before" studies. Thirty minutes will be allotted for smoking 3 cigarettes consecutively. After finishing the last one, the experimental or "after" studies will be carried out. The following studies will be accomplished before and after smoking or before and during the injection of intravenous nicotine (nicotine bitartrate). Each patient will act as his own control.

1. Cerebral Blood Flow using the N_2O Technique (Kety, S. S. The Quantitative Determination of Cerebral Blood Flow in Man, Methods in Medical Research, Year Book Publishers, Chicago, 1948, Vol. I, pp 204-215).
2. Arterial and Cerebral Venous O_2 and CO_2 Contents by the manometric technique of Van Slyke and Neill, (Peters, J. A. and Van Slyke, D. D., Quantitative Clinical Chemistry, Williams and Wilkins, Baltimore, 1931).
3. Arterial and Cerebral Venous pH measured anaerobically at room temperature by means of a glass electrode and Cambridge potentiometer. Values will be corrected to $37^\circ C$ by the factors of Rosenthal (Effect of Temperature on pH of Blood and Plasma in Vitro, J. Biol. Chem., 1948, 173, 25).
4. Arterial and Cerebral Venous pCO_2 will be calculated by means of the nomograms of Peters and Van Slyke, (Peters, J. A. and Van Slyke, D. D., Quantitative

Clinical Chemistry, Williams and Wilkins, Baltimore, 1931).

The following studies will be accomplished at short intervals every 2 to 4 minutes before, during, and after smoking.

5. Intraarterial Pulse Pressure Wave Recordings. A Sanborn Electromanometer and Twin Viso Recorder will be used.
6. Electrocardiograms (standard 12 leads with multiple recordings of Lead V_4). The Twin Viso Recorder will be used.
7. Electroencephalograms with a Grass Encephalograph. Cerebral O_2 consumption and cerebral vascular resistance will be calculated from this data.

6. Budget Plan:

Salaries	\$ 6,200.00
Expendable Supplies	1,600.00
Permanent Equipment	1,200.00
Overhead	1,000.00
Other	-----

TOTAL \$10,000.00

7. Anticipated Duration of Work:

One Year.

8. Facilities and Staff Available:

1. Source of Human Subjects

2. Equipment

- 2 Van Slyke Manometric Gas Apparatus
- 1 Cambridge pH Meter
- 2 Grass Electroencephalographs
- 1 Hamilton Electromanometer (Sanborn)
- 1 Twin Viso Recorder (Sanborn)
- Equipment for Cerebral Blood Flow Studies including gas mixtures, manifolds, syringes, and so on.

3. Staff

- (1) Richard L. Wechsler, M. D., Clinical Physiologist, 8 years experience in field of cerebral blood flow and metabolism.
- (2) Yale David Koskoff, M. D., Ph. D., Director of Montefiore Hospital Institute of Research.
- (3) Philip Brostoff, M. D. Cardiologist.
- (4) Chaskiel Grossman, M. D., Electroencephalographer.
Will read electroencephalograms.
- (5) Richard Abrams, Ph. D. (Biochemistry) Associate Director,
Montefiore Hospital Institute of Research.

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- (6) Mr. Philip Louis Woolf, Research Assistant, trained in techniques necessary for accomplishing project.

9. Additional Requirements:

None.

10. Additional Information (Including relation of work to other projects and other sources of supply):

Similar studies are in progress evaluating various anticholinergic compounds.

Signature

Richard L. Wachsler M.D.
Director of Project

Y. D. Kosloff M.D.
Business Officer of the Institution

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